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Benzyl Benzoate
Interim Registration Review Decision
Case Number 4013

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Approved by: _____

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I. INTRODUCTION

This document is Environmental Protection Agency's (EPA or Agency) Interim Registration Review Decision (ID) for benzyl benzoate, also known as benylate (PC Code 009501), case 4013, and is being issued pursuant to 40 CFR §§ 155.56 and 155.58. Registration review case 4013 includes three PC Codes: benzyl benzoate (PC Code 009501), benzyl alcohol (PC Code 009502), and sodium benzoate (PC Code 009103). The only current conventional registrations for this case are under PC Code 009501, benzyl benzoate, which is the focus of this review. Recently the active ingredient sodium benzoate (PC Code 009103) was registered by the Office of Pesticide Programs' Antimicrobials Division for in-container control of bacteria, mold and fungi in industrial and household products in October 2020 (Product: Kalaguard™ SB, EPA Registration Number 91212-1) and is not included in this registration review since it was recently evaluated. Another active ingredient, benzoic acid (PC Code 009101), has antimicrobial uses as a preservative of food-grade lubricating oils in industrial facilities, which are in a different case and covered separately by the Office of Pesticide Programs' Antimicrobials Division (docket number: EPA-HQ-OPP-2010-0692; case 5107; available online at www.regulations.gov). A registration review decision is the Agency's determination whether a pesticide continues to meet, or does not meet, the standard for registration in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The Agency may issue, when it determines it to be appropriate, an interim registration review decision before completing a registration review. Among other things, the interim registration review decision may determine that new risk mitigation measures are necessary, lay out interim risk mitigation measures, identify data or information required to complete the review, and include schedules for submitting the required data, conducting the new risk assessment and completing the registration review. Additional information on benzyl benzoate can be found in the EPA's public docket (EPA-HQ-OPP-2015-0597) at www.regulations.gov.

FIFRA, as amended by the Food Quality Protection Act (FQPA) of 1996, mandates the continuous review of existing pesticides. All pesticides distributed or sold in the United States must be registered by EPA based on scientific data showing that they will not cause unreasonable risks to human health or to the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess and reduce risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically re-evaluates pesticides to make sure that as these changes occur, products in the marketplace can continue to be used safely. Information on this program is provided at http://www.epa.gov/pesticide-reevaluation. In 2006, the Agency implemented the registration review program pursuant to FIFRA § 3(g) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration.

EPA is issuing an ID for benzyl benzoate so that it can move forward with aspects of the registration review that are complete. In the case of benzyl benzoate, the Agency has reached a "no effects" determination for listed species for the registered uses of this chemical and based on this, consultation with the Services is not needed. Given that the threshold for effects to listed species is lower than non-listed species, EPA determined that effects to all non-target, non-listed

species are unlikely as well. This *de minimis* ecological risk determination for benzyl benzoate was posted to the docket at the time of the Final Work Plan in 2016. The Agency will complete endocrine screening for benzyl benzoate, pursuant to the Federal Food, Drug, and Cosmetic Act (FFDCA) § 408(p), before completing registration review. See Appendix A for additional information on the endocrine screening for the benzyl benzoate registration review.

Benzyl benzoate is registered as a miticide. The only current active conventional registrations in this case include a technical product and an associated end-use product containing benzyl benzoate. The mode of action for benzyl benzoate is classified as unknown.[1] The end-use product is formulated as pressurized liquid spray for the treatment of sarcoptic mange mites on dogs. This product is registered for indoor use in residential and commercial sites. A Reregistration Eligibility Decision (RED) was issued for benzyl benzoate in June 2007.

This document is organized in five sections: the *Introduction*, which includes this summary and a summary of public comments and EPA's responses; *Use and Usage*, which describes how and why benzyl benzoate is used and summarizes data on its use; *Scientific Assessments*, which summarizes EPA's risk and benefits assessments, updates or revisions to previous risk assessments, and provides broader context with a discussion of risk characterization; the *Interim Registration Review Decision*, which describes the mitigation measures to address risks of concern and the regulatory rationale for EPA's ID; and, lastly, the *Next Steps and Timeline* for completion of this registration review.

A. Updates since the Proposed Interim Decision was Issued

In October 2020, the EPA published the Proposed Interim Decision (PID) for benzyl benzoate. No comments were received and there are no updates from the PID.

B. Summary of Benzyl Benzoate Registration Review

Pursuant to 40 CFR § 155.50, the EPA formally initiated registration review for benzyl benzoate with the opening of the registration review docket for the case. The following summary highlights the docket opening and other significant milestones that have occurred thus far during the registration review of benzyl benzoate.

- April 2016 - The *Benzyl Benzoate Preliminary Work Plan* (PWP*)*, *Benzyl Benzoate: Human Health Scoping Document in Support of Registration Review*, and *Benzyl Benzoate – Registration Review Preliminary Ecological Risk Assessment and De Minimus Risk Memo* were posted to the docket for a 60-day public comment period.

- November 2016 - The *Benzyl Benzoate Final Work Plan* (FWP) was issued. No public comments were received on the PWP.

[1] University of Hertfordshire, 2018. "Pesticide Properties Data Base: Benzyl benzoate." University of Hertfordshire. PPDB, General Chemical Information. https://sitem.herts.ac.uk/aeru/ppdb/en/Reports/1473.htm

- March 2017 - A Generic Data Call-In for benzyl benzoate (GDCI-009501-1607) was issued for data needed to conduct the registration review risk assessments. The single data requirement was waived, and the GDCI is satisfied.

- October 2020 - *Benylate* (*Benzyl Benzoate): Human Health Draft Risk Assessment for Registration Review, Benzyl Benzoate Proposed Interim Registration Review Decision*, and *Benylate: Revised Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment* were published in the benzyl benzoate registration review docket for a 60-day public comment period. During the 60-day public comment period for the benzyl benzoate proposed interim decision, which opened on October 23, 2020 and closed on December 22, 2020 the Agency did not receive any public comments.

- March 2021 - The Agency is announcing the *Benzyl Benzoate Interim Registration Review Decision,* which is available in the docket for benzyl benzoate.

II. USE AND USAGE

Benzyl benzoate is a miticide that was first registered in the United States in 1958. It is a member of the benzyl derivatives family, which also includes non-pesticidal compounds used in food flavors and fragrances and may occur naturally in various foods. Based on the registered use pattern, it is designated as a non-food use pesticide.

There are two active pesticide product registrations containing benzyl benzoate, a technical product, EPA Registration No. 2781-54 and an associated end-use product, EPA Registration No. 2781-51. The end-use product, Sardex II, is a ready-to-use pressurized spray registered for use to control the mites that cause sarcoptic mange in dogs. The Agency was not able to identify any usage data for the product. The mode of action for benzyl benzoate is unknown.

The benzyl benzoate end-use product is registered for use indoors in residential and commercial sites. Label directions advise the user to clip hair around all affected areas, wash thoroughly with soap and water, rinse, and wipe dry or allow the animal to dry before application. The product is then sprayed on the affected areas, rubbed in slightly, allowed to dry, then applied a second time. Applications can be repeated every seven days until the condition clears.

III. SCIENTIFIC ASSESSMENTS

A. Human Health Risks

A summary of the Agency's human health risk assessment is presented below. The Agency prepared a qualitative risk assessment in support of the registration review of benzyl benzoate. The toxicological database for benzyl benzoate was recently reevaluated, and no effects were seen at doses relevant for human health risk assessment. Because no endpoints were identified, the Agency could not conduct a quantitative assessment. For additional details on the assessment, see *Benylate* (*Benzyl Benzoate) Human Health Draft Risk Assessment for Registration Review*, which is available in the public docket.

1. Risk Summary and Characterization

Benzyl benzoate is not registered for use on food crops or livestock and is registered for use indoors only, so no food or drinking water exposure is expected from its use as a pesticide. Residential and occupational exposures are expected from the dog mange spray treatment. Residential handler (adult) exposures are expected from the application of the product and adults and children may be exposed from contact with previously treated dogs. Occupational exposures are also expected from the professional application of mange spray to affected dogs.

Dietary (Food + Water) Risks

No dietary exposure (food or drinking water) is expected from the currently registered miticide use of benzyl benzoate.

Residential Handler, Residential Post-Application, Bystander, and Occupational Risks

While the use of benzyl benzoate as a treatment for mange has the potential to result in residential handler, residential post-application, and occupational exposures, no human health hazard has been identified. Therefore, there are no risks of concern associated with residential or occupational exposures to pesticide products containing benzyl benzoate.

Aggregate

Since no dietary exposure is expected and residential risks were not estimated due to the lack of human health hazard, aggregate exposures are not expected from benzyl benzoate products and have not been assessed.

Cumulative Risks

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to benzyl benzoate and any other substances and benzyl benzoate does not appear to produce a toxic metabolite produced by other substances. Therefore, EPA has not assumed that benzyl benzoate has a common mechanism of toxicity with other substances.

2. Human Incidents and Epidemiology

The 2016 incident summary, *Benzyl Benzoate: Tier I (Scoping) Review of Human incidents and Epidemiology*, noted that all incidents reported for benzyl benzoate up until 2015 were associated with the use of carpet treatments targeting dust mites, not the treatment of sarcoptic mange. The carpet treatment registrations have been cancelled since 2005. The incident summary from 2020, *Benylate: Revised Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment,* notes that for the Main IDS for the five years from January 1, 2015 to March 26, 2020, there were no incidents reported that involved the active ingredient benylate (benzyl benzoate). For Aggregate IDS for the five years from January 1, 2015 to January 26, 2021, there was one incident reported involving benylate (benzyl benzoate). A query of SENSOR-Pesticides

from 2012-2015 identified one case involving benylate. This incident was classified as minor severity. The Agency will continue to monitor the incident information. Additional analyses will be conducted if ongoing human incident monitoring indicates a concern.

3. Tolerances

Given the currently registered use pattern, benzyl benzoate is designated as a non-food use chemical and therefore tolerances are not established for residues on food or feed commodities in the U.S. There are currently no established Canadian or Codex maximum residue limits (MRLs) established for residues of benzyl benzoate.

4. Human Health Data Needs

There are no data deficiencies for benzyl benzoate.

B. Ecological Risks

A summary of the Agency's ecological risk assessment is presented below. The Agency prepared a qualitative risk assessment in support of the registration review of benzyl benzoate. For additional details on the ecological assessment for benzyl benzoate, see the *Benzyl Benzoate – Registration Review Preliminary Ecological Risk Assessment and De Minimis Risk Memo*, which is available in the public docket.

1. Risk Summary and Characterization

Based on the registered use pattern for benzyl benzoate, the Agency determined that a quantitative registration review risk assessment was not necessary. In addition, the Agency has determined that the registered uses of benzyl benzoate present *de minimis* risks to non-target and threatened and endangered species, based on a number of factors:

- Use patterns are limited to indoor and dog uses.
- Extent of use is limited.
- There is a low likelihood of outdoor or water exposure.
- Benzyl benzoate has a very low toxicity to non-target organisms overall.
- Conclusions about non-target organism toxicity are corroborated by ECOSAR, a database that facilitates the characterization of ecotoxicity on the basis of structural activity relationships when case-specific data are insufficient.

EPA has reached a "no effects" determination for listed species for registered uses of benzyl benzoate. Given that the threshold for effects to listed species is lower than for non-listed species, EPA has determined that effects to all non-target, non-listed species are not reasonably expected to occur from the registered uses of benzyl benzoate.

2. Ecological and Environmental Fate Data Needs

There are no data deficiencies for benzyl benzoate.

C. Benefits

Sarcoptic mange, also known as scabies, is a severe skin condition caused by parasitic mites that feed on and under the skin of host dogs and other mammals. Scabies can be transferred between animals and humans. Mange treatments for dogs are largely administered by veterinarians as professional diagnosis is always recommended prior to treating mange[2]. Benzyl benzoate is one of several over-the-counter products available for control of the mites causing sarcoptic mange in dogs.

IV. INTERIM REGISTRATION REVIEW DECISION

A. Risk Mitigation and Regulatory Rationale

The Agency has not identified any risks of concern associated with the use of the pesticide benzyl benzoate as currently registered. The most recent end-use product label text for EPA Registration No. 2781-51, on file with the Agency (from 2013) is in the form of a "notification" and appears to comport with the comments the Agency made on the earlier stamped, accepted label (from 2010). Based on the findings of this registration review, as described in Section III, risk mitigation measures or label changes are not needed for benzyl benzoate products at this time.

B. Interim Registration Review Decision

In accordance with 40 CFR §§ 155.56 and 155.58, the Agency is issuing this ID. Except for the Endocrine Disruptor Screening Program (EDSP) component of the case, the Agency has made the following interim decision: (1) no additional data are needed at this time; (2) no risks of concern have been identified for the use of benzyl benzoate, and therefore changes to the affected registrations and their labeling are not needed at this time; and (3) benzyl benzoate products continue to satisfy the FIFRA standard for registration.

In this ID, the Agency is making no human health or environmental safety findings associated with the EDSP screening of benzyl benzoate. EPA has reached a "no effects" determination for listed species for registered uses of benzyl benzoate. The Agency's final registration review decision for benzyl benzoate will be dependent upon an EDSP FFDCA § 408(p) determination.

C. Data Requirements

The Agency does not anticipate calling-in additional data for the registration review of benzyl benzoate at this time.

[2] Ward, E. and A. Panning, 2018. "Sarcoptic Mange in Dogs." Veterinary Centers of America (VCA) Hospitals, 2018. Available at: https://vcahospitals.com/know-your-pet/mange-sarcoptic-in-dogs

V. NEXT STEPS AND TIMELINE

A. Interim Registration Review Decision

A Federal Register Notice will announce the availability of this ID for benzyl benzoate. EPA is issuing this interim registration review decision for benzyl benzoate, however a final decision for benzyl benzoate may be issued without the Agency having previously issued an interim decision. A final decision on the benzyl benzoate registration review case will occur after an EDSP FFDCA § 408(p) determination.

Appendix A: Endocrine Disruptor Screening Program

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where the EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA § 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. The Agency has reviewed all of the assay data received for the List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets. A second list of chemicals identified for EDSP screening was published on June 14, 2013,[3] and includes some pesticides scheduled for Registration Review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors. Benzyl benzoate is not on either list. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit the EPA website.[4]

In this ID, EPA is making no human health or environmental safety findings associated with the EDSP screening of benzyl benzoate. Before completing this registration review, the Agency will make an EDSP FFDCA § 408(p) determination.

[3] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
[4] https://www.epa.gov/endocrine-disruption